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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,323	03/16/2001	Daniel Keith Burns	PU3562USW	9629
23347	7590	12/05/2001		
DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY GLAXOSMITHKLINE FIVE MOORE DR. PO BOX 13398 DURHAM, NC 27709-3398			EXAMINER	JOHANSEN, DIANA B
			ART UNIT	PAPER NUMBER
			1655	

DATE MAILED: 12/05/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/787,323	<b>Applicant(s)</b> BURNS ET AL
	<b>Examiner</b> Diana B. Johannsen	<b>Art Unit</b> 1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply is less than thirty (30) days, and a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 16 April 2001.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 1-13 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-13 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
 If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
 a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.      4) Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.  
 5) Notice of Informal Patent Application (PTO-152)  
 6) Other: *Notice to Comply* .

**DETAILED ACTION**

***Priority***

1. This application is a 371 of PCT/US99/21092, filed September 14, 1999, and claims the benefit of U.S. provisional application 60/100,491, filed September 16, 1998, and U.S. provisional application no. 60/100,704, filed September 17, 1998. The International Search Report and International Preliminary Examination Report for PCT/US99/21092 have been received.

***Specification***

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Applicant is requested to return a copy of the attached Notice to Comply with the response to this Office action.

3. The specification also fails to comply with one or more of the requirements of 37 CFR § 1.821 through 1.825 because the specification recite sequences that lack description by a sequence identifier set forth in the "Sequence Listing" as required by 37 CFR § 1.821(d). See, for example, p. 5. Appropriate corrections for compliance are required.

4. The disclosure is objected to because of the following informalities: the specification recites descriptions of Figures 1-3; however, no such Figures are present in the application. Appropriate correction is required.

It is noted that Figures were not provided either by applicant or by the U.S. Receiving Office, and that it appears that Figures 1-3 were not published with international publication WO 00/15833. However, it is also noted that a figure was published on the cover page of WO 00/15833, suggesting that Figures 1-3 may have been included with PCT/US99/21092 and erroneously excluded from the present application file. Accordingly, it is requested that applicant clarify the status of the Figures.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:  
  
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.  
  
6. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 are indefinite for failing to recite a final process step that clearly relates back to the preamble. The claims are drawn to a method "of identifying a nucleic acid," yet recite a final process step of loading sequencing reaction products onto a sequencing gel. The claims do not set forth how loading "two or more" short sequencing products allows one to "identify" a nucleic acid. Thus, it is unclear as to

whether the claims are intended to be drawn to a method of loading or running a sequencing gel, or to methods of "identifying" a nucleic acid. Further, the term "identifying" is vague and indefinite, as it does not apprise one of skill in the art as to what information is to be ascertained with respect to a nucleic acid. Further, it is unclear as to whether the term "identifying" may encompass solely mental steps of "identification," or whether this language is limited to active method steps. The claims should be amended so as to clarify the actual, active process steps necessary to accomplish "identification" of a nucleic acid.

Claims 1-6 are indefinite over the recitation of the phrases "two or more short sequencing reaction products," "a first sequencing reaction product," and "a second short sequencing reaction product" in claim 1. It is unclear, e.g., as to whether Applicant intends for the term "first sequencing reaction product" to refer to one of the "two or more short sequencing reaction products," or to another, additional "sequencing reaction product." Thus, it is unclear as to whether the instant claims require one or more additional "short sequencing reaction products" in addition to the "first sequencing reaction product" and the "second short sequencing reaction product." Clarification is required.

Claims 2-3 are indefinite over the recitation of the phrase "the sequencing reaction product." Claim 1, from which claims 2-3 depend, recites more than one "sequencing reaction product." Accordingly, it is unclear as to how claims 2-3 are intended to modify claim 1(i.e., do the claims limit each reaction product, the "first sequencing reaction product," the "second short sequencing reaction product"?).

Claims 6-12 are indefinite for failing to recite a final process step that clearly relates back to the preamble. The claims are drawn to a "method of determining the nucleotide sequence of a selected portion of a nucleic acid," yet recite a final process step of "analyzing the first sequencing reaction product." The claims do not set forth how "analyzing" a sequencing reaction product results in "determining the nucleotide sequence" of a portion of a nucleic acid, and the term "analyzing" is sufficiently broad so as to encompass solely mental steps of "analysis." Accordingly, it is not clear whether the instant claims are intended to be drawn to methods of determining the sequence of a portion of a nucleic acid, or to methods of "analyzing" a sequencing reaction product. Clarification is required.

Claims 6-13 are indefinite over the recitation of the term "selected enzyme" in claims 6, 8, and 13, and the term "selected portion" in claim 6. It is unclear as to how the term "selected" is intended to modify the structure and/or function of an enzyme of a "portion". In other words, how would a "selected" enzyme or portion differ from an enzyme or portion? Clarification is required.

Claims 6-12 are indefinite over the recitation of the phrase "the inserts of the library" in claim 6. There is insufficient antecedent basis for this limitation in the claims, as claim 6 does not previously refer to "inserts" of a library.

Claim 7 is indefinite over the recitation of the phrase "analyzed sequentially on the same analysis run." First, it is unclear as to what is encompassed by the language "analyzed sequentially," and as to what actual method steps might be required in order to accomplish "sequential analysis." Second, there is insufficient antecedent basis for

the limitation "the same analysis run," as the claims do not previously refer to an "analysis run" or to a "same analysis run." Clarification is required.

Claim 9 is indefinite over the recitation of the limitation "the selected restriction enzyme." There is insufficient antecedent basis for this limitation in the claims, as the claims do not previously refer to a "selected restriction enzyme."

Claims 10-12 are indefinite over the recitation of the limitation "the analysis...." In each of the claims. It is unclear as to how these limitations on the "analyzing" step of the method result in or otherwise contribute to "determining the nucleotide sequence" of a portion of a nucleic acid. The claims should be amended so as to clarify what actual steps are carried out, and so as to set forth how such steps result in sequence determination.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kinzler et al (U.S. Patent No. 5,695,937).

The claim is drawn to a kit comprising "an enzyme that cuts at least 1 base downstream of a selected enzyme recognition site" and a "set of oligonucleotide linkers comprising a recognition site for the selected enzyme." It is noted that the intended use of a product or structure recited in a claim preamble is not accorded patentable weight (see MPEP 2111.02).

Kinzler et al teach a method for the "serial analysis of gene expression" that requires the use of type IIS restriction enzymes and oligonucleotide linkers comprising recognition sites for type IIS restriction enzymes (see entire reference). Kinzler et al teach kits comprising sets of linkers wherein the linkers "comprise a restriction endonuclease site for cleavage of DNA at a site distant from the restriction endonuclease restriction site" (col 8, lines 1-18). Kinzler et al further teach the use of type IIS restriction enzymes, and teach that such enzymes cleave "at a site distant from or outside of the recognition site" that is "up to 20 bp away from their asymmetric recognition sites" (col 5, lines 51-60). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the kits of Kinzler et al so as to have included therein both oligonucleotide linkers and type IIS

Art Unit: 1655

restriction enzymes that recognize the recognition sites present in the linkers, as well as other reagents required for the practice of Kinzler et al's method. As both the linkers and the restriction enzymes are necessary for the practice of Kinzler et al's method, an ordinary artisan would have been motivated to have made such a modification in order to have provided practitioners with all the reagents necessary to carry out the method of Kinzler et al, for the advantages of convenience, efficiency, and cost-effectiveness.

### ***Conclusion***

10. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Schellenberg et al (U.S. Patent No. 5,449,604) teach sequencing of short DNA fragments (col 3, line 67-col 4, line 2; col 12, lines 29-30; col 13, lines 56-59). Sapolsky et al (U.S. Patent No. 5,710,000) disclose methods of "capturing" oligonucleotide sequences adjacent to type IIS restriction sites, and disclose that the sequences of captured oligonucleotides are preferably determined by hybridization (see entire reference). Brenner et al (Proc. Natl. Acad. Sci. USA 86:8902-8906 [11/1989]) disclose a DNA fingerprinting method in which termini of fragments generated by digestion with type IIS restriction enzymes are sequenced (see entire reference).

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 703/305-0761. The examiner can normally be reached on Monday-Friday, 7:00 am-3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on 703/308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are 703/305-3014 for regular communications and 703/305-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703/308-0196.

Diana B. Johannsen  
December 3, 2001

  
W. Gary Jones  
Supervisory Patent Examiner  
Technology Center 1600